

herein) is utilized in the compositions and methods of the present invention for both overcoming control of sterol importation uptake and increasing sterol biosynthesis (increasing metabolic flux). Another example of a gene that confers such activity is SUT 1 (SEQ ID NO:413; Karst et al., 2001). In another specific embodiment, two separate alleles which confer both phenotypes, or a different single allele which confers both phenotypes, are utilized *in lieu* of the *upc2-1* allele.

**Paragraph 155:**

In a specific embodiment, at least one *ERG9* (squalene synthase) (GenBank Accession No. X59959; SEQ ID NO:409) modification is generated by standard means in the art to create a “bottleneck” in the pathway, thereby permitting the shuttling of increased amounts of FPP to the bioengineered diterpene pathway. One means to partially block a transformation is achieved by employing a temperature-sensitive mutation which allows examination of impaired enzymatic activity without the adverse effect of completely blocking metabolism. Temperature-sensitive mutations weaken an enzyme's secondary structure. The resultant protein becomes especially sensitive to thermal denaturation, thereby rendering its activity temperature-sensitive. A temperature-sensitive *ERG9* mutation (Karst *et al.*, 1971) was incorporated by genetic cross into the yeast comprising a chromosomal nucleic acid sequence encoding a GGPP synthase under the control of an inducible promoter. A strain comprising the *erg9-1* temperature-sensitive mutation was purchased from American Type Culture Collection (ATCC 64031) and tetrads from the genetic crosses were selected by observing growth rate at various temperatures as compared to the control strain EHY1.